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(54) COMPONENT B AS CICATRIZANT

KOMPONENTE B ALS WUNDHEILENDES MITTEL

COMPOSANT B UTILISE COMME CICATRISANT

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(73) Proprietor: **Applied Research Systems ARS Holding N.V.**
Curacao (AN)

(72) Inventors:
- **BORRELLI, Francesco**
  I-00179 Rome (IT)
- **DONINI, Silvia**
  I-00186 Rome (IT)
- **MARTELLI, Fabrizio**
  I-00162 Rome (IT)
- **MASTRANGELI, Renato**
  I-00146 Rome (IT)

(74) Representative: **Gervasi, Gemma, Dr.**
NOTARBARTOLO & GERVASI Srl,
Corso di Porta Vittoria, 9
20122 Milano (IT)

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Description

[0001] The present invention relates to the use of Component B as cicatrizant, in particular in the treatment of wounds, ulcers and other traumatic lesions to any of the tissues in the body.

[0002] Component B is a 81-amino acid protein originally isolated from human urine. The human gene has been cloned and expressed in CHO cells as recombinant human Component B. The molecule has a molecular weight of about 8.9 kD. It has been thoroughly described in WO 94/14959.

[0003] Such protein contains ten cysteines and bears a motif typical of serine protease enzymes. Sequence alignment to a protein data bank has shown some homologies of Component B with known molecules such as CD59, urokinase receptor (uPA-R) and some venom toxins.

[0004] Data obtained by the Applicant from the study of organ and tissue distribution in mice showed that eye, lung and skin are the sites in which Component B RNA is mainly expressed. In human tissues, Component B was found to be highly expressed in the squamous epithelia and mucosae, such as skin, oesophagus and exocervix, as determined by immunohistochemistry. Finally, EGF has been found to induce the expression of Component B RNA in human squamous epidermoid A431 cells.

[0005] In WO 94/14959 Component B is reported to have antiinflammatory, anticoagulant and antitumoral activity, as well as an activity as inihibitor of the binding of TGF-α to its receptor.

[0006] The Applicant has now found that Component B is also useful as cicatrizant, and it is, therefore, in particular, useful in the treatment of wounds, ulcers and other traumatic lesions to any of the tissues in the body.

[0007] Therefore, the main object of the present invention is the use of Component B for the manufacture of a pharmaceutical composition useful as cicatrizant, in particular in the treatment of wounds, ulcers and other traumatic lesions to any of the tissues in the body.

[0008] A further object of this invention is the use of component B for the manufacture of a medicament for a method of treatment of wounds, ulcers and other traumatic lesions to any of the tissues in the body, in which an effective amount of Component B, together with a pharmaceutically acceptable excipient is to be administered.

[0009] For the methods of preparation of Component B and for its amino acid sequence, reference is made to the disclosure of WO 94/14959.

[0010] The administration of the active ingredient may be by oral, intravenous, intramuscular, subcutaneous or topical route. Other routes of administration, which may establish the desired blood levels of the respective ingredients, are comprised by the present invention.

[0011] For the human therapy the preferred doses are 1 mg/kg or less for the systemic administration and 4 $\mu g/cm^2$ or less for the topical administration.

[0012] The invention will now be described by means of the following Examples, which should not be construed as in any way limiting the present invention. The Examples will refer to the Figures as specified here below.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013]

Figure 1: the effect of the intravenous administration of Component B in comparison with that of betametasone (Bentelan®) on the experimental wound healing is shown. In particular, the results of Experiment 1 are summarised. Test drugs were administered daily for 6 consecutive days from day 0 (the day of wound induction) through 5.

Figure 2: the effect of the intravenous administration of Component B (batch 004-001b) in comparison with that of betametasone (Bentelan®) on the experimental wound healing is shown. In particular, the results of Experiment 2 are summarised. Test drugs were administered daily for 6 consecutive days from day 0 (the day of wound induction) through 5.

Figure 3: the effect of the topical application of Component B (batch 004-001) on the experimental wound healing is shown. In particular, the results of Experiment 3 are summarised. Test drugs were topically applied for 5 consecutive days from day 0 (the day of wound induction) through 4.

Figure 4: the effect of the topical application of bovine serum albumin on the experimental wound healing is shown. In particular, the results of Experiment 4 are summarised. Test drugs were topically applied for 5 consecutive days from day 0 (the day of wound induction) through 4.

Figure 5: the sigmoidal dose response analysis applied to the results of Experiment 1 is reported. The effect of the intravenous administration of Component B (batches 004-001 and 004-001b, indicated as "001" and "001b", respectively) and betametasone (Bentelan ®) on the experimental wound healing is, therefore, statistically evaluated on the basis of the results of Experiment 1.

Figure 6: the sigmoidal dose response analysis applied to the results of Experiment 2 is reported. The effect of the intravenous administration of Component B (batch 004-001b, indicated as "001b") and betametasone (Bente-

lan®) on the experimental wound healing is, therefore, statistically evaluated on the basis of the results of Experiment 2.

Figure 7: the sigmoidal dose response analysis applied to the cumulated results of Experiments 1 and 2 is reported. The effect of the intravenous administration of Component B (batch 004-001b) on the experimental wound healing is, therefore, statistically evaluated on the basis of the combination of the results of Experiments 1 and 2.

Figure 8: the sigmoidal dose response analysis applied to the cumulative frequency, relative to combination of Experiments 1 and 2 is reported. The effect of Component B (batch 004-001b) is so evaluated.

Figure 9: the sigmoidal dose response analysis applied to the results of Experiment 3 is reported. The effect of the topical and intravenous administration of Component B (batch 004-001) on the experimental wound healing is, therefore, statistically evaluated on the basis of the results of Experiment 3.

Figure 10: : the sigmoidal dose response analysis applied to the results of Experiment 4 is reported. A comparison of the effect between buffer and BSA in wound reduction is, therefore, statistically evaluated on the basis of the results of Experiment 4.

EXAMPLES

Materials

Animals

[0014] SPF CD-I mice of both sexes, purchased from Charles River Italia (Calco, Como. Italy), were used for the experiments after an acclimatisation period of at least seven days under controlled environmental conditions (temperature: 22±2°C; humidity: 55±10% and a light/dark cycle of 12 hours).

Test compounds

[0015]

- rec-hComponent B batch 004-001 (sulphated form) and 004-001b (non-sulphated form) expressed in CHO cells and produced essentially as described in WO 94/14959.
- Commercial preparation of betametasone (Bentelan®) from Glaxo (Verona, Italy).
- Sodium chloride 0.9 % (saline), from Baxter (Trieste, Italy).
- Bovine serum albumin (BSA), fraction V supplied by Sigma Chemical Co. (St. Louis MO, USA).

Methods

Experimental full-thickness wound healing

[0016] The method used was that suggested by J.J.P. Morton and M.H. Malone (Morton J.J.P. and Malone M.H., Arch. Int. Pharmacodyn. 196:117, 1972), who used this procedure for the evaluation of a number of drugs for their vulnerary activity in rats.

[0017] For the present study of Component B, the original method was suitably modified to be used in mice, as follows.

[0018] A circular ink mark (1 cm diameter) was impressed on the dorsal region of male mice (30-35 g, 6-7 week-old), and the skin of this marked area (including *panniculus carnosus* and adherent tissues) was excised using surgical scissors and forceps. The wound was then blotted dry with gauze pads until haemostasis occurred. On day 0, i. e. the day of surgery, longitudinal, transverse and two diagonal measurements (relative to the vertebral column) were made of the diameter of the wound to the nearest 0.1 mm using a direct reading caliper. The exact points of measurements were preserved by marking the adjacent skin with indelible ink. Subsequent wound measurements were made every other day except on Sunday up to complete wound closure. Both surgery and measurements were made under light ether anaesthesia of the mice.

[0019] The area of each wound was obtained by multiplying the square of its mean diameter by 0.7854. Per cent wound closure was then calculated relative to day 0. The mean per cent wound closure values for each measurement day were tabulated for each experimental group and the closure time 50% (CT_{50}) interpolated.

Systemic treatment

[0020] Two experiments (Experiments 1 and 2) were performed. In the second experiment, on each measurement day, the measurements were performed by the same operator who was unaware of the treatment schedules. In each

experiment the animals were divided into 4 groups and treated according to the following schedule.

Group number	1st experiment	2nd experiment
1	Saline 10 ml/kg, i.p.	Saline 10 ml/kg, i.v.
2	Component B 004-001, 1 mg/kg, i.v.	Component B 004-001b, 0.1 mg/kg, i.v.
3	Component B 004-001b, 1 mg/kg, i.v.	Component B 004-001b, 1 mg/kg, i.v.
4	Betametasoue, 1 mg/kg, i.p.	Betametasone, 1 mg/kg, i.v.

[0021] The animals were treated once a day for 6 consecutive days. The body weight of the animals was monitored for the whole duration of the study.

Topical treatment

[0022] In a further experiment (Experiment 3) the effect of the topical application of different doses of Component B (batch 004-001) were studied by using the already described procedure for wound induction following the treatment schedule reported in the table herebelow.

Group number	Treatment
1	Phosphate buffer 0.05 ml, topically
2	Component B 004-001, 1 μg, topically
3	Component B 004-001, 2 μg, topically
4	Component B 004-001, 4 μg, topically
5	Component B 1 mg/kg, i.v.

[0023] The solutions of the test product were applied (volume 0.05 ml) onto the wounds on days 1 and 2, whereas in the successive days, when the scab had been formed, they were injected underneath the scab by a syringe equipped with a 25G needle.

[0024] Component B administered i.v. at the dose of 1 mg/kg, has been used as positive reference standard.

[0025] To rule out the possibility of aspecific effects of topical application of a proteic solution, in a parallel experiment the effect of BSA, at the same molar concentrations (8.8×10^{-6}M) as Component B, was assayed topically in comparison to phosphate buffer (Experiment 4).

Results

Wound healing

[0026] Figure 1 reports the data of the first Experiment, in which the activity of two batches (004-001 and 004-001b) of Component B were compared. Both of them were capable of accelerating the cicatrization process, their effects being already evident after 1 day of treatment. CT_{50}, i.e. the time when 50% wound reduction occurs, is 3.0 and 3.4 days, respectively, these values being not statistically different. By contrast, CT_{50}'s of 7.8 and 7.2 days were observed with betametasone (Bentelan®) and saline, respectively (see the paragraph entitled "Statistical Analysis").

[0027] In the second Experiment (Figure 2) two doses of Component B (batch 004-001b) were studied. At the highest dose, I mg/kg, the CT_{50} was 3.7 days whereas it was of 6.6 days at the lowest dose (0.1 mg/kg). The saline and betametasone treated groups displayed CT_{50}'s of 9.1 and 10 days, respectively (see the paragraph entitled "Statistical Analysis").

[0028] The positive effect of Component B on wound healing was also confirmed by another index, namely ET_{50}, indicating the time when 50% of the animals showed complete wound closure (see the paragraph entitled "Statistical Analysis").

[0029] The results of the experiment where Component B (batch 004-001) was applied topically onto the wound (Experiment 3), are reported in Figure 3. The compound was studied at doses of 1. 2 and 4 μg/day for 5 consecutive days. All doses assayed were capable of enhancing the wound healing process as compared to controls. In particular, doses of 2 and 4 μg provided CT_{50} values of 3.8 and 4.4, respectively, which are comparable to that found (3.9) with 1 mg/kg of Component B given i.v. With the lowest dose (1 μg), a CT_{50} value of 5.3 days was observed, which is higher

than those obtained with the other two topical doses, but still significantly different from controls (see the paragraph entitled "Statistical Analysis").

[0030] These data suggest that a dose of 2 µg, topically applied on the wound, produces the maximal effect and that 1 µg is still effective in enhancing the cicatrization process.

[0031] In order to verify whether the positive effect of Component B on the wound healing process is a specific characteristic of the product, a parallel experiment was carried out, in which the effect of BSA, at the same molar concentration of Component B, was compared to that of phosphate buffer (Experiment 4). These data are reported in Figure 4. CT_{50}'s of 9.9 and 7.9 days were recorded with BSA and phosphate buffer, respectively. The above values are not significantly different (see the paragraph entitled "Statistical Analysis"), thus indicating that a standard protein solution, like BSA, does not influence the cutaneous wound repair.

[0032] The individual data ofthese experiments are reported in Tables 1A-4B.

Statistical Analysis

Statistical strategy

[0033] The statistical analysis was aimed at comparing the effect over the time of two preparations of Component B (Comp. B) both *vs* saline and the reference drug Bentelan.

[0034] Furthermore, the effects of the systemic and the topical administration of one preparation of Component B have been also evaluated.

[0035] In accordance with the treatment protocol the effect of the test drugs was studied considering the entire observation period.

[0036] The wound reduction experiment was repeated twice in order to confirm the Comp B effect at different dose levels.

Statistical test

[0037] The Sigmoidal Dose Response Analysis for the evaluation of the CT_{50} (i.e. the time when the wound area is reduced by 50%) was used as the statistical test (see Finney D. J., Biometrics, 32, pp. 721-40, 1976).

Statistical units

[0038]

1) Wound reduction (CT_{50}): Average percentage of variation vs average basal values.
2) Cumulative Frequency (ET_{50}) : Cumulative frequency of animals showing a complete wound closure at each time point.

Groups of treatment (Exp. No 1)

[0039]

1 - Saline - 10 ml/kg/day, i.p. for 6 days
2 - Bentelan - I mg/kg/day, i.p. for 6 days
3 - CompB 004-001- 1 mg/kg/day, i.v. for 6 days
4 - CompB 004-001b- 1 mg/kg/day. i.v. for 6 days

Groups of treatment (Exp. No 2)

[0040]

1 - Saline - 10 ml/kg/day, i.v. for 6 days
2 - Bentelan - 1 mg/kg/day, i.v. for 6 days
3 - CompB 004-001b- 0.1 mg/kg/day. i.v. for 6 days
4 - CompB 004-001b- 1 mg/kg/day, i.v. for 6 days

Groups of treatment (Exp. No 3)

[0041]

1 - Phosphate buffer- 50 µl/day, topical for 5 days
3 - CompB 004-001- 1 µg/day, topical for 5 days
3 - CompB 004-001- 2 µg/day, topical for 5 days
4 - CompB 004-001- 4 µg/day, topical for 5 days
5 - CompB 004-001- 1 mg/kg/day, i.v. for 5 days

Groups of treatment (Exp. No 4)

[0042]

1 -Phosphate buffer - 50 µl/day, topical for 5 days
2 -Bovine serum albumin (BSA) - 50 µl/day (8.8×10^{-6}M), topical for 5 days

Treatment schedule (for Experiments 1, 2, 3 and 4)

[0043]

Phase 1: Repeated treatment days according to the above treatment-group description.
Phase 2: Observation period up to the day of complete wound closure.

Results of the statistical analysis

[0044] The diagrams (sigmoidal dose response analysis) reported in Figures 5-10 summarise the effect of the test drugs using as the variable the wound area.

Experiment. 1

[0045] Reference is made to Figure 5.
[0046] The results of the sigmoidal dose response analysis (CT_{50}) applied to the wound area, relative to experiment 1, are reported in the following table.

Test Drug	CT_{50} (days)	Confidence Limits	R^2
Saline	7.2	6.2 - 8.3	0.96
Bentelan 1 mg/kg	7.8	6.9 - 8.8	0.97
CompB 004-001 1 mg/kg	3.0	2.5 - 3.7	0.97
CompB 004-001b 1 mg/kg	3.4	2.8 - 4.1	0.97

Experiment 2

[0047] Reference is made to Figure 6.
[0048] The results of the sigmoidal dose response analysis (CT_{50}) applied to the wound area, relative to experiment 2 are reported in the following table.

Test Drug	CT_{50} (days)	Confidence Limits	R^2
Saline	9.1	8.4 - 9.9	0.98
Bentelan 1 mg/kg	10.0	9.6 - 10.4	0.99
CompB 004-001b 0.1 mg/kg	6.6	5.5 - 7.7	0.94
CompB 004-001b 1 mg/kg	3.7	2.8 - 4.8	0.92

Combination of Experiments 1 and 2

[0049] Reference is made to Figure 7.

[0050] The results obtained from the combination of the data of treatment groups common to both experiments I and 2, i.e. saline vs CompB-004-001b 1 mg/kg are summarised.

[0051] In addition, the frequency over the time of the animals showing complete closure of the wound was also evaluated (by Sigmoidal Dose-Response Analysis) from the cumulated data of Experiments 1 and 2.

[0052] The results of the sigmoidal dose response analysis (CT_{50}) applied to the wound area, relative to the combination of experiments 1 and 2, are reported in the following table.

Test Drug	CT_{50} (days)	Confidence Limits	R^2
Saline	8.2	7.5 - 8.9	0.95
CompB 004-001b 1 mg/kg	3.5	3.0-4.1	0.95

[0053] For the cumulative frequency, reference is made to Figure 8.

[0054] The results of the sigmoidal dose response analysis (ET_{50}) applied to the cumulative frequency, relative to the combination of experiments 1 and 2, are reported in the following table.

Test Drug	ET_{50} (days)	Confidence Limits	R^2
Saline	16.1	154 - 16.9	0.98
CompB 004-001b 1 mg/kg	11.7	11.2 - 12.1	0.99

[0055] In conclusion, the comparison among CT_{50} values and among ET_{50} values is a good estimate of the effect of each test drug on the experimental model.

[0056] Both CompB-001 (1 mg/kg, i.v.) and CompB-001b (dose levels 0.1 mg/kg and 1 mg/kg, i.v.) were found to be statistically different from saline and Bentelan in Experiments 1 and 2. The results of the combination of treatment groups common to Experiments 1 and 2 confirm the effect of the i.v. route of administration with CompB 1 mg/kg.

Experiment 3

[0057] Reference is made to Figure 9.

[0058] A further set of experiments was performed in which the product was topically applied. The intravenous route was used as positive reference standard. The data were analysed using the same statistical models as above.

[0059] The results of the sigmoidal dose response analysis (CT_{50}) applied to the wound area, relative to experiment 3, are reported in the following table.

Test Drug	CT_{50} (days)	Confidence Limits	R^2
Phosphate Buffer	8.3	7.3 - 9.5	0.96
CompB-001 1 mcg topical	5.3	4.1 - 6.9	0.91
CompB-001 2 mcg topical	3.8	2.9 - 4.9	0.92
CompB-001 4 mcg topical	4.4	3.4 - 5.6	0.92
CompB-001 1 mg/kg i.v.	3.9	3.0 - 5.2	0.92

[0060] In conclusion, topical administration of CompB-001b showed, at all doses tested, a wound reduction (CT_{50}) significantly different from phosphate buffer.

Experiment 4

[0061] Reference is made to Figure 10.

[0062] The diagram reports the comparison between topical application of phosphate buffer and BSA in wound reduction in order to rule out possible aspecific effects of Component B.

[0063] The results of the sigmoidal dose response analysis (CT_{50}) applied to the wound area, relative to Experiment 4, are reported in the following table.

Test Drug	CT_{50} (days)	Confidence Limits	R^2
Buffer	7.9	7.2 - 8.7	0.98
BSA	9.9	8.5 - 11.4	0.95

[0064] The above results did not show any differences between the topical application of phosphate buffer and BSA.

Conclusions of all the study

[0065] The interesting result of this study is the activity of Component B in the cicatrization process both when administered intravenously or by topical application. The experimental model used in this study is directly related to the human trauma counterpart and is predictive for the application of Component B in the healing of traumatic lesions of the skin and in plastic and reconstructive surgery of mucosae and epithelia.

Table 1A:

Wound healing data - Experiment 1								
Comp B 004-001 : 1 mg/kg, i.v.								
Day 0	*Day 1*		*Day 3*		*Day 5*		*Day 7*	
area	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.622	0.529	-14.9518	0.318	-48.8746	0.135	-78.2958	0.06	-90.3537
0.813	0.745	-8.36408	0.566	-30.3813	0.604	-25.7073	0.483	-40.5904
0.761	0.701	-7.88436	0.341	-55.1905	0.201	-73.5874	0.111	-85.4139
0.644	0.418	-35.0932	0.289	-55.1242	0.125	-80.5901	0.103	-84.0062
0.825	0.549	-33.4545	0.266	-67.7576	0.133	-83.8788	0.049	-94.0606
0.724	0.624	-13.8122	0.432	-40.3315	0.313	-56.768	0.251	-65.3315
0.679	0.697	2.650957	0.402	-40.7953	0.214	-68.4831	0.114	-83.2106
0.769	0.478	-37.8414	0.412	-46.4239	0.3	-60.9883	0.137	-82.1847
0.709	0.48	-32.299	0.374	-47.2496	0.285	-59.8025	0.195	-72.4965
Mean ± S.D.								
0.727	0.580	-20.117	0.378	-48.014	0.257	-65.345	0.167	-77.516
0.071	0.116	14.736	0.090	10.711	0.150	17.734	0.134	16.334

Day 9		*Day 11*		*Day 14*				
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*			
0.039	-93.7299	0.031	-95.0161	0	-100			
0.288	-64.5756	0.104	-87.2079	0.039	-95.203			
0.06	-92.1156	0.009	-98.8173	0	-100			
0.046	-92.8571	0	-100	0	-100			
0.043	-94.7879	0	-100	0	-100			
0.173	-76.105	0	-100	0	-100			
0.084	-87.6289	0.104	-84.6834	0.13	-80.8542			
0.1	-86.9961	0.06	-92.1977	0	-100			
0.196	-72.3554	0	-100	0	-100			

Table 1A: (continued)

Wound healing data - Experiment 1								
Comp B 004-001 : 1 mg/kg, i.v.								
Day 9		*Day 11*		*Day 14*				
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*			
Mean ± S.D.								
0.114	-84.572	0.034	-95.325	0.019	-97.340			
0.086	10.896	0.044	6.007	0.044	6.382			
Day 16		*Day 18*						
area	*% variat.*	*area*	*% variat.*					
0	-100	0	-100					
0.007	-99.139	0	-100					
0	-100	0	-100					
0	-100	0	-100					
0	-100	0	-100					
0	-100	0	-100					
0.046	-93.2253	0	-100					
0	-100	0	-100					
0	-100	0	-100					
Mean ± S.D.								
0.006	-99.152	0	-100.000					
0.015	2.241	0.000	0.000					

Table 1B:

Wound healing data - Experiment 1								
Comp B 004-001b : 1 mg/kg, i.v.								
Day 0	*Day 1*		*Day 3*		*Day 5*		*Day 7*	
area	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.535	0.505	-5.60748	0.402	-24.8598	0.273	-48.972	0.162	-69.7196
0.656	0.611	-6.85976	0.194	-70.4268	0.083	-87.3476	0.017	-97.4085
0.647	0.631	-2.47295	0.365	-43.5858	0.3	-53.6321	0.114	-82.3802
0.813	0.508	-37.5154	0.363	-55.3506	0.177	-78.2288	0.142	-82.5338
0.781	0.622	-20.3585	0.385	-50.7042	0.289	-62.9962	0.169	-78.3611
0.785	0.656	-16.4331	0.435	-44.586	0.334	-57.4522	0.205	-73.8854
0.777	0.559	-28.0566	0.397	-48.906	0.361	-53.5393	0.259	-66.6667
0.724	0.618	-14.6409	0.528	-27.0718	0.455	-37.1547	0.323	-55.3867
0.747	0.756	1.204819	0.36	-51.8072	0.244	-67.336	0.256	-65.7296
0.903	0.729	-19.2691	0.561	-37.8738	0.27	-70.0997	0.175	-80.6202
Mean ± S.D.								
0.737	0.620	-15.001	0.399	-45.517	0.279	-61.676	0.182	-75.269
0.103	0.083	112.021	0.100	13.438	0.101	14.717	0.086	11.665

Day 9		*Day 11*		*Day 14*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0.109	-79.6262	0.075	-85.9813	0.073	-86.3551	
0	-100	0	-100	0	-100	
0.057	-91.1901	0.054	-91.6538	0	-100	
0.11	-86.4699	0	-100	0	-100	
0.069	-91.1652	0.046	-94.1101	0	-100	
0.146	-81.4013	0.008	-98.9809	0	-100	

Table 1B: (continued)

Wound healing data - Experiment 1						
Comp B 004-001b : 1 mg/kg, i.v.						
Day 9		*Day 11*		*Day 14*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0.179	-76.9627	0.026	-96.6538	0	-100	
0.235	-67.5414	0.017	-97.6519	0	-100	
0.196	-73.7617	0	-100	0	-100	
0.077	-91.4729	0.049	-94.5736	0	-100	
Mean ± S.D.						
0.118	-83.959	0.028	-95.961	0.007	-98.636	
0.072	9.844	0.027	4.533	0.023	4.315	
Day 16		*Day 18*				
area	*% variat.*	*area*	*% variat.*			
0.028	-94.7664	0	-100			
0	-100	0	-100			
0	-100	0	-100			
0	-100	0	-100			
0	-100	0	-100			
0	-100	0	-100			
0	-100	0	-100			
0	-100	0	-100			
0	-100	0	-100			
0	-100	0	-100			
Mean ± S.D.						
0.003	-99.477	0	-100.000			

Table 1B: (continued)

Wound healing data - Experiment 1					
Comp B 004-001b : 1 mg/kg, i.v.					
Day 16			Day 18		
area	% variat.		area	% variat.	
0.009	1.655		0.000	0.000	

Table 1C:

Wound healing data - Experiment 1								
Bentelan 1mg/kg, i.p.								
Day 0	*Day 1*		*Day 3*		*Day 5*		*Day 7*	
area	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.671	0.634	-5.51416	0.64	-4.61997	0.507	-24.4411	0.265	-60.5067
0.76	0.737	-3.02632	0.667	-12.2368	0.535	-29.6053	0.445	-41.4474
0.703	0.737	4.836415	0.618	-12.091	0.277	-60.5974	0.246	-65.0071
0.885	0.898	1.468927	0.697	-21.2429	0.735	-16.9492	0.759	-14.2373
0.788	0.762	-3.29949	0.799	1.395939	0.594	-24.6193	0.626	-20.5584
0.701	0.662	-5.56348	0.705	0.570613	0.493	-29.6719	0.46	-34.3795
0.654	0.631	-3.51682	0.666	1.834862	0.466	-28.7462	0.491	-24.9235
Mean ± S.D.								
0.737	0.723	-2.088	0.685	-6.627	0.515	-30.661	0.470	-37.294
0.080	0.094	3.847	0.059	8.820	0.138	13.935	0.183	19.567

Day 9		*Day 11*		*Day 14*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0.201	-70.0447	0.199	-70.3428	0.056	-91.6542	
0.352	-53.6842	0.339	-55.3947	0.091	-88.0263	
0.215	-69.4168	0.084	-88.0512	0	-100	
0.551	-37.7401	0.331	-62.5989	0.176	-80.113	
0.535	-32.1066	0.275	-65.1015	0	-100	
0.302	-56.9187	0.162	-76.8902	0	-100	
0.263	-59.7859	0.173	-73.5474	0.031	-95.2599	
Mean ± S.D.						
0.346	-54.242	0.223	-70.275	0.051	-93.579	

Table 1C: (continued)

Wound healing data - Experiment 1						
Bentelan 1mg/kg, i.p.						
Day 9		*Day 11*		*Day 14*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0.144	14.609	0.095	10.627	0.065	7.554	
Day 16		*Day 18*				
area	*% variat.*	*area*	*% variat.*			
0.011	-98.3607	0	-100			
0.008	-98.9474	0	-100			
0	-100	0	-100			
0.031	-96.4972	0	-100			
0	-100	0	-100			
0	-100	0	-100			
0.031	-95.2599	0	-100			
Mean ± S.D.						
0.012	-98.438	0.000	-100.000			
0.014	1.891	0.000	0.000			

Table 1D:

Wound healing data - Experiment 1								
Saline 10 ml/kg, i.p.								
Day 0	*Day 1*		*Day 3*		*Day 5*		*Day 7*	
area	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.937	0.929	-0.854	0.636	-32.1238	0.398	-57.524	0.275	-70.651
0.997	0.948	-4.915	0.675	-32.2969	0.601	-39.7192	0.463	-53.5607
0.833	0.856	2.761	0.854	2.521008	0.793	-4.80192	0.749	-10.084
0.804	0.796	-0.995	0.797	-0.87065	0.767	-4.60199	0.751	-6.59204
0.697	0.825	18.364	0.605	-13.1994	0.644	-7.60402	0.64	-8.17791
0.729	0.745	2.195	0.626	-14.1289	0.454	-37.7229	0.385	-47.1879
0.618	0.645	4.369	0.518	-16.1812	0.327	-47.0874	0.209	-66.1812
0.72	0.594	-17.500	0.528	-26.6667	0.287	-60.1389	0.189	-73 75
Mean ± S.D.								
0.792	0.792	0.428	0.655	-16.618	0.534	-32.400	0.458	-42.023
0.127	0.126	9.996	0.119	13.199	0.195	23.444	0.232	29.254

Day 9		*Day 11*		*Day 14*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0.127	-86.4461	0.139	-85.1654	0	-100	
0.366	-63.2899	0.297	-70.2106	0.039	-96.0883	
0.608	-27.0108	0.339	-59.3037	0.151	-81.8727	
0.541	-32.7114	0.36	-55.2239	0.1	-87.5622	
0.512	-26.5423	0.347	-50.2152	0.128	-81.6356	
0.331	-54.5953	0.238	-67.3525	0.012	-98.3539	
0.132	-78.6408	0	-100	0	-100	
0.085	-88.1944	0	-100	0	-100	

Table 1D: (continued)

Wound healing data - Experiment 1						
Saline 10 ml/kg, i.p.						
Day 9		*Day 11*		*Day 14*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
Mean ± S.D.						
0.338	-57.179	0.215	-73.434	0.054	-93.189	
0.206	26.106	0.151	19.519	0.063	8.172	
Day 16		*Day 18*				
area	*% variat.*	*area*	*% variat.*			
0	-100	0	-100			
0	-100	0	-100			
0.02	-97.599	0	-100			
0	-100	0	-100			
0.026	-96.2697	0	-100			
0	-100	0	-100			
0	-100	0	-100			
0	-100	0	-100			
Mean ± S.D.						
0.006	-99.234	0.000	-100.000			
0.011	1.463	0.000	0.000			

Table 2A:

Wound heating data - Experiment 2								
Comp B 004-001b: 0.1 mg/kg, i.v.								
Day 0	*Day 1*		*Day 3*		*Day 5*		*Day 7*	
area	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.679	0.58	-14.5803	0.561	-17.3785	0.566	-16.6421	0.347	-48.8954
0.693	0.677	-2.3088	0.635	-8.36941	0.603	-12.987	0.493	-28.86
1.002	0.759	-24.2515	0.84	-16.1677	0.749	-25.2495	0.525	-47.6048
0.833	0.677	-18.7275	0.701	-15.8463	0.584	-29.892	0.401	-51.8607
0.671	0.597	-11.0283	0.458	-31.7437	0.412	-38.5991	0.282	-57.9732
0.651	0.526	-19.2012	0.604	-7.21966	0.556	-14.5929	0.424	-34.8694
0.682	0.755	10.70381	0.452	-33.7243	0.512	-24.9267	0.242	-64.5161
0.817	0.601	-26.4382	0.55	-32.6805	0.486	-40.5141	0.408	-50.0612
0.693	0.538	-22.3665	0.418	-39.6825	0.307	-55.6999	0.246	-64.5022
0.799	0.58	-27.4093	0.58	-27.4093	0.461	-42.3029	0.418	-47.6846
0.777	0.686	-11.7117	0.563	-27.5418	0.433	-44.2728	0.282	-63.7066
Mean ± S.D.								
0.754	0.634	-15.211	0.578	-23.433	0.515	-31.425	0.379	-49.683
0.105	0.081	11.420	0.120	10.927	0.1171	13.897	0.098	11.427

Day 9		*Day 11*		*Day 14*		*Day 16*	
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.347	-48.8954	0.196	-71.134	0.009	-98.6745	0	-100
0.309	-55.4113	0.139	-79.9423	0.039	-94.3723	0.012	-98.27
0.454	-54.6906	0.146	-85.4291	0.058	-94.2116	0.018	-98.20
0.206	-75.2701	0.053	-93.6375	0	-100	0	-100
0.238	-64.5306	0.142	-78.8376	0.04	-94.0387	0	-100

Table 2A: (continued)

Wound heating data - Experiment 2							
Comp B 004-001b: 0.1 mg/kg, i.v.							
Day 9		*Day 11*		*Day 14*		*Day 16*	
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.329	-49.4624	0.216	-66.8203	0.15	-76.9585	0.052	-92.01
0.179	-73.7537	0.046	-93.2551	0	-100	0	-100
0.282	-65.4835	0.177	-78.3354	0	-100	0	-100
0.231	-66.6667	0.122	-82.3954	0	-100	0	-100
0.409	-48.811	0.203	-74.5932	0	-100	0	-100
0.225	-71.0425	0.105	-86.4865	0.008	-98.9704	0	-100
Mean ± S.D.							
0.292	-61.274	0.140	-80.988	0.027636	-96.111	0.007	-98.953
0.087	10.150	0.057	8.449	0.046	6.842	0.016	2.408
Day 18		*Day 21*		*Day 23*			
area	*% variat.*	*area*	*% variat.*	*area*	*% variat*		
0	-100	0	-100	0	-100		
0	-100	0	-100	0	-100		
o	-100	0	-100	0	-100		
0	-100	0	-100	0	-100		
0	-100	0	-100	0	-100		
0	-100	0	-100	0	-100		
0	-100	0	-100	0	-100		
0	-100	0	-100	0	-100		
0	-100	0	-100	0	-100		
0	-100	0	-100	0	-100		
0	-100	0	-100	0	-100		

Table 2A: (continued)

Wound heating data - Experiment 2								
Comp B 004-001b: 0.1 mg/kg, i.v.								
Day 18		Day 21			Day 23			
area	% variat.	area	% variat.		area	% variat		
Mean ± S.D.								
0	-100.000	0	-100.000		0	-100.000		
0.000	0.000	0.000	0.000		0.000	0.000		

Table 2B:

Wound healing data - Experiment 2								
Comp B 004-001b: 1 mg/kg, i.v.								
Day 0	Day 1		Day 3		Day 5		Day 7	
area	area	% variat.	area	% variat.	area	% variat.	area	% variat.
0.769	0.601	-21.8466	0.455	-40.8322	0.297	-61.3784	0.121	-84.2653
0.763	0.525	-31.1927	0.493	-35.3866	0.464	-39.1874	0.451	-40.8912
0.964	0.712	-26.1411	0.358	-62.8631	0.287	-70.2282	0.134	-86.0996
0.712	0.573	-19.5225	0.421	-40.8708	0.563	-20.927	0.179	-74.8596
0.763	0.59	-22.6737	0.266	-65.1376	0.155	-79.6855	0.054	-92.9227
0.793	0.747	-5.80076	0.415	-47.6671	0.334	-57.8815	0.185	-76.6709
0.785	0.451	-42.5478	0.238	-69.6815	0.199	-74.6497	0.168	-78.5987
0.747	0.701	-6.15797	0.458	-38.6881	0.398	-46.7202	0.29	-61.178
0.873	0.765	-12.3711	0.73	-16.3803	0.667	-23.5968	0.515	-41.008
0.979	0.867	-11.4402	0.667	-31.8693	0.594	-39.3258	0.448	-54.239
0.833	0.716	-14.0456	0.594	-28.6915	0.528	-36.6146	0.395	-52.581
1.225	0.72	-41.2245	0.528	-56.898	0.458	-62.6122	0.384	-68.6531
Mean ± S.D								
0.8505	0.664	-21.247	0.469	-44.581	0.412	-51.067	0.277	-67.664
0.145	0.117	12.337	0.148	16.249	0.161	19.536	0.156	17.540

Day 9		*Day 11*		*Day 14*		*Day 16*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0.056	-92.7178	0.044	-94.2783	0	-100		0 -100	
0.344	-54.9148	0.146	-80.865	0	-100		0 -100	
0.03	-96.888	0	-100	0	-100		0 -100	
0.171	-75.9831	0.021	-97.0506	0	-100		0 -100	

Table 2B: (continued)

Wound healing data - Experiment 2								
Comp B 004-001b: 1 mg/kg, i.v.								
Day 9		*Day 11*		*Day 14*		*Day 16*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0.038	-95.0197	0	-100	0	-100		0 -100	
0.061	-92.3077	0.024	-96.9735	0	-100		0 -100	
0.039	-95.0318	0	-100	0	-100		0 -100	
0.138	-81.5261	0.038	-94.913	0	-100		0 -100	
0.344	-60.5956	0.192	-78.0069	0	-100		0 -100	
0.186	-81.001	0.019	-98.0592	0	-100		0 -100	
0.238	-71.4286	0.159	-80.9124	0	-100		0 -100	
0.392	-68	0.148	-87.9184	0	-100		0 -100	
Mean ± S.D.								
0.170	-80.451	0.066	-92.415	0	-100.000	0	-100.000	
0.133	14.429	0.073	8.257	0 000	0.000	0.000	0.000	

Table 2C:

Wound healing data - Experiment 2								
Bentelan 1 mg/kg, i.v.								
Day 0	*Day 1*		*Day 3*		*Day 5*		*Day 7*	
area	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.789	0.813	3.041825	0.767	-2.78834	0.615	-22.0532	0.565	-28.3904
0.769	0.831	8.062419	0.846	10.013	0.833	8.322497	0.751	-2.3407
0.805	0.741	-7.95031	0.751	-6.70807	0.763	-5.21739	0.525	-34.7826
0.751	0.86	14.51398	0.825	9.853529	0.997	32.75632	0.586	-21.9707
0.842	0.864	2.612827	0.858	1.900238	0.773	-8.19477	0.675	-19.8337
0.856	0.739	-13.6682	0.769	-10.1636	0.712	-16.8224	0.636	-25.7009
0.651	0.679	4.301075	0.69	5.990783	0.626	-3.84025	0.555	-14.7465
0.769	0.679	-11.7035	0.636	-17.2952	0.656	-14.6944	0.622	-19.1157
0.763	0.86	12.71298	0.869	13.89253	0.777	1.834862	0.751	-1.57274
0.675	0.679	0.592593	0.769	13.92593	0.709	5.037037	0.655	-2.96296
0.805	0.667	-17.1429	0.69	-14.2857	0.72	-10.559	0.622	-22.7329
0.644	0.886	37.57764	0.809	25.62112	0.565	-12.2671	0.551	-14.441
Mean ± S.D.								
0.760	0.775	2.746	0.773	2.496	0.729	-3.808	0.625	-17.383
0.070	0.086	14.999	0.073	13.020	0.115	14.627	0.074	10.667

Day 9		*Day 11*		*Day 14*		*Day 16*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0.317	-59.8226	0.258	-67.3004	0.151	-80.8619	0.081	-89.7338	
0.424	-44.8635	0.344	-55.2666	0.222	-71.1313	0.11	-85.6957	
0.457	-43.2298	0.312	-61.2422	0.181	-77.5155	0.066	-91.8012	
0.755	0.532623	0.587	-21.8375	0.369	-50.8655	0.216	-71.2383	
0.545	-35.2732	0.315	-62.5891	0.117	-86.1045	0.026	-96.9121	
0.43	-49.7664	0.259	-69.743	0.118	-86.215	0.035	-95.9112	
0.396	-39.1705	0.24	-63.1336	0.071	-89.0937		0 -100	
0.433	-43.6931	0.309	-59 8179	0.212	-72.4317	0.025	-96.749	
0.594	-22.1494	0.433	-43.2503	0.092	-87.9423	0.016	-97.903	
0.415	-38.5185	0.325	-51.8519	0.203	-69.9259	0.036	-94.6667	
0.499	-38.0124	0.302	-62.4845	0.157	-80.4969	0.013	-98.3851	
0.312	-51.5528	0.124	-80.7453	0.033	-94.8758		0 -100	
Mean ± S.D.								
0.465	-38.793	0.317	-58.272	0.161	-78.955	0.052	-93.250	
0.122	15.500	0.112	14.749	0.088	11.768	0.061	8.146	

Table 2C: (continued)

Wound healing data - Experiment 2						
Bentelan 1 mg/kg, i.v.						
Day 18		*Day 21*		*Day 23*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0.02	-97.4651	0	-100	0	-100	
0.059	-92.3277	0.047	-99.417	0	-100	
0.01	-98.7578	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0.015	-98.0494	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
Mean ± S.D.						
0.009	-98.883	0.004	-99.951	0.000	-100.000	
0.017	2.250	0.014	0.168	0.000	0.000	

Table 2D:

Wound healing data - Experiment 2								
Saline 10 ml/kg, i.v.								
Day 0	*Day 1*		*Day 3*		*Day 5*		*Day 7*	
area	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.58	0.594	2.413793	0.535	-7.75862	0.538	-7.24138	0.466	-19.6552
0.773	0.755	-2.32859	0.763	-1.29366	0.584	-24.4502	0.561	-27.4256
0.735	0.785	6.802721	0.779	5.986395	0.735	0	0.622	-15.3741
0.805	0.666	-17.2671	0.655	-18.6335	0.615	-23.6025	0.385	-52.1739
0.701	0.629	-10.271	0.629	-10.271	0.546	-22.1113	0.493	-29.6719
0.686	0.671	-2.18659	0.584	-14.8688	0.535	-22.0117	0.478	-30.3207
0.601	0.59	-1.83028	0.58	-3.49418	0.536	-10.8153	0.451	-24.9584
0.759	0.747	-1.58103	0.72	-5.13834	0.627	-17.3913	0.551	-27.4045
Mean ± S.D.								
0.705	0.680	-3.281	0.656	-6.934	0.590	-15.953	0.501	-28.373
0.080	0.075	7.423	0.090	7.796	0.069	8.978	0.074	10.892

Day 9		*Day 11*		*Day 14*		*Day 16*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0.325	-43.9655	0.206	-64.4828	0.206	-64.4828	0.104	-82.069	
0.339	-56.1449	0.238	-69.2109	0.181	-76.5847	0.116	-84.9935	
0.436	-40.6803	0.187	-74.5578	0.197	-73.1973	0.067	-90.8844	
0.408	-49.3168	0.28	-65.2174	0.216	-73.1677	0.047	-94.1615	
0.369	-47.3609	0.249	-64.4793	0.238	-66.0485	0.036	-94.8645	
0.246	-64.1399	0.273	-60.2041	0.175	-74.4898	0	-100	
0.282	-53.0782	0.297	-50.5824	0.201	-66.5557	0.048	-92.0133	
0.469	-38.2082	0.377	-50.3294	0.24	-68.3794	0.036	-95.2569	

Table 2D: (continued)

Wound healing data - Experiment 2								
Saline 10 ml/kg, i.v.								
Day 9		*Day 11*		*Day 14*		*Day 16*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
Mean ± S.D.								
0.359	-49.112	0.263	-62.383	0.20675	-70.363	0.057	-91.780	
0.076	8.541	0.059	8.460	0.024	4.524	0.038	5.807	
Day 18		*Day 21*		*Day 23*				
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*			
0.027	-95.3448	0	-100	0	-100			
0.041	-94.696	0.027	-96.5071	0	-100			
0	-100	0	-100	0	-100			
0	-100	0	-100	0	-100			
0	-100	0	-100	0	-100			
0	-100	0	-100	0	-100			
0	-100	0	-100	0	-100			
0.017	-97.7602	0	-100	0	-100			
Mean ± S.D.								
0.011	-98.475	0.003	-99.563	0.000	-100.000			
0.016	2.275	0.010	1.235	0.000	0.000			

Table 3A:

Wound healing data - Experiment 3								
Component B (004-001) 1μg								
Day 0	*Day 1*		*Day 3*		*Day 5*		*Day 7*	
area	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.746	0.709	-4.95979	0.584	-21.7158	0.477	-36.059	0.305	-59.1153
0.92	0.659	-28.3696	0.404	-56.087	0.304	-66.9565	0.242	-73.6957
0.687	0.618	-10.0437	0.466	-32.1689	0.444	-35.3712	0.41	-40.3202
0.818	0.822	0.488998	0.503	-38.5086	0.388	-52.5672	0.372	-54.5232
0.742	0.571	-23.0458	0.451	-39.2183	0.399	-46.2264	0.372	-49.8652
0.716	0.677	-5.44693	0.636	-11.1732	0.548	-23.4637	0.503	-29.7486
0.833	0.638	-23.4094	0.487	-41.5366	0.402	-51.7407	0.377	-54.7419
0.659	0.52	-21.0926	0.49	-25.6449	0.425	-35.5083	0.332	-49.6206
0.738	0.724	-1.89702	0.571	-22.6287	0.491	-33.4688	0.466	-36.8564
0.705	0.545	-22.695	0.233	-66.9504	0.195	-72.3404	0.152	-78.4397
Mean ± S.D.								
0.756	0.648	-14.047	0.471	-35.563	0.407	-45.370	0.353	-52.693
0.079	0.091	10.696	0.112	16.759	0.100	15.606	0.103	15.277

Day 9		*Day 11*		*Day 14*		*Day 16*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0.41	-45.0402	0.129	-82.7078	0.056	-92.4933	0	-100	
0.181	-80.3261	0.09	-90.2174	0.008	-99.1304	0	-100	
0.366	-46.7249	0.15	-78.1659	0.099	-85.5895	0	-100	
0.345	-57.824	0.198	-75.7946	0.063	-92.2983	0.033	-95.9658	
0.271	-63.4771	0.12	-83.8275	0	-100	0	-100	
0.475	-33.6592	0.267	-62.7095	0.02	-97.2067	0	-100	

Table 3A: (continued)

Wound healing data - Experiment 3								
Component B (004-001) 1μg								
Day 9		*Day 11*		*Day 14*		*Day 16*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0.35	-57.9832	0.204	-75.5102	0.045	-94.5978	0	-100	
0.246	-62.6707	0.11	-83.308	0.017	-97.4203	0	-100	
0.401	-45.664	0.18	-75.6098	0.031	-95.7995	0.008	-98.916	
0.11	-84.3972	0.189	-73.1915	0.008	-98.8652	0.008	-98.8652	
Mean ± S.D.								
0.316	-57.777	0.164	-78.104	0.035	-95.340	0.005	-99.375	
0.112	15.939	0.054	7.507	0.031	4.340	0.010	1.284	

Day 18		*Day 21*		*Day 23*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
Mean ± S.D.						
0	-100.000	0	-100	0	-100	

Table 3A: (continued)

Wound healing data - Experiment 3						
Component B (004-001) 1µg						
Day 18		Day 21		Day 23		
area	% variat.	area	% variat.	area	% variat.	
0.000	0.000	0.000	0.000	0.000	0.000	

Table 3B:

Wound healing data - Experiment 3								
Phosphate buffer								
Day 0	*Day 1*		*Day 3*		*Day 5*		*Day 7*	
area	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.785	0.75	-4.4586	0.747	-4.84076	0.285	-63.6943	0.271	-65.4777
0.673	0.768	14.1159	0.731	8.618128	0.626	-6.98366	0.612	-9.06389
0.785	0.772	14.71025	0.747	-4.84076	0.487	-37.9618	0.439	-44.0764
0.902	0.902	0	0.862	-4.43459	0.754	-16.408	0.739	-18.071
0.785	0.742	-5.47771	0.766	-2.42038	0.535	-31.8471	0.531	-32.3567
0.694	0.694	0	0.672	-3.17003	0.448	-35.4467	0.433	-37.6081
0.733	0.846	15.4161	0.743	1.364256	0.506	-30.9686	0.487	-33.5607
0.666	0.742	11.41141	0.778	16.81682	0.535	-19.6697	0.475	-28.6787
0.768	0.765	-0.39063	0.687	-10.5469	0.312	-59.375	0.322	-58.0729
Mean ± S.D.								
0.755	0.776	5.036	0.748	-0.384	0.499	-33.595	0,479	-36.330
0.074	0.062	8.698	0.055	8.301	0.145	18.710	0.141	17.828

Day 9		*Day 11*		*Day 14*		*Day 16*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0.26	-66.879	0.221	-71.8471	0.107	-86.3694	0.042	-94.6497	
0.522	-22.4368	0.217	-67.7563	0.057	-91.5305	0	-100	
0.401	-48.9172	0.374	-52.3567	0.15	-80.8917	0.096	-87.7707	
0.601	-33.3703	0.324	-64.0798	0.103	-88.5809	0.038	-95.7871	
0.535	-31.8471	0.358	-54.3949	0.15	-80.8917	0.04	-94.9045	
0.382	-44.9568	0.238	-65.7061	0.128	-81.5562	0.053	-92.3631	
0.46	-37.2442	0.3	-59.0723	0.1	-86.3574	0.058	-92.0873	

Table 3B: (continued)

Wound healing data - Experiment 3								
Phosphate buffer								
Day 9		*Day 11*		*Day 14*		*Day 16*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0.255	-61.7117	0.264	-60.3604	0.101	-84.8348	0.102	-84.6847	
0.297	-61.3281	0.269	-64.974	0.025	-96.7448	0	-100	
Mean ± S.D.								
0.413	-45.410	0.285	-62.283	0.102	-86.418	0.048	-93.583	
47.474	15.475	0.058	6.308	0.041	5.300	0.036	5.084	
Day 18		*Day 21*		*Day 23*				
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*			
0	-100	0	-100	0	-100			
0	-100	0	-100	0	-100			
0	-100	0	-100	0	-100			
0.008	-99.1131	0	-100	0	-100			
0.012	-98.4713	0.012	-98.4713	0	-100			
0.041	-94.0922	0.008	-98.8473	0	-100			
0.008	-98.9086	0	-100	0	-100			
0.092	-86.1862	0.095	-85.7357	0	-100			
0	-100	0	-100	0	-100			
Mean ± S.D.								
0.018	-97.419	0.013	-98.117	0.000	-100.000			
0.031	4.611	10.031	4.680	0.000	0.000			

Table 3C:

Wound healing data - Experiment 3								
Component B (004-001) 4 μg								
Day 0	*Day 1*		*Day 3*		*Day 5*		*Day 7*	
area	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.826	0.604	-26.8765	0.512	-38.0145	0.293	-64.5278	0.248	-69.9758
0.731	0.635	-13.1327	0.515	-29.5486	0.371	-49.2476	0.324	-55.6772
0.785	0.659	-16.051	0.538	-31.465	0.43	-45.2229	0.358	-54.3949
0.803	0.742	-7.59651	0.601	-25.1557	0.49	-38.9788	0.427	-46.8244
0.727	0.691	-4.95186	0.676	-7.01513	0.509	-29.9862	0.468	-35.6259
0.785	0.581	-25.9873	0.506	-35.5414	0.379	-51.7197	0.278	-64.586
0.866	0.523	-39.6074	0.329	-62.0092	0.218	-74.8268	0.161	-81.4088
0.757	0.666	-12.0211	0.582	-23.1176	0.407	-46.2351	0.319	-57.86
0.799	0.526	-34.1677	0.319	-60.0751	0.236	-70.4631	0.169	-78.8486
0.81	0.568	-29.8765	0.430	-46.9136	0.374	-53.8272	0.292	-63.9506
Mean ± S.D.								
0.789	0.620	-21.027	0.501	-35.886	0.371	-52.504	0.304	-60.915
0.043	0.072	11.842	0.114	16.883	0.098	13.987	0.099	13.999

Day 9		*Day 11*		*Day 14*		*Day 16*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0.187	-77.3608	0.106	-87.1671	0.02	-97.5787	0	-100	
0.208	-71.5458	0.132	-81.9425	0	-100	0	-100	
0.223	-71.5924	0.102	-87.0064	0	-100	0	-100	
0.283	-64.7572	0.126	-84.3088	0.01	-98.7547	0	-100	
0.311	-57.2215	0.145	-80.055	0	-100	0	-100	
0.188	-76.051	0.008	-98.9809	0	-100	0	-100	

Table 3C: (continued)

Wound healing data - Experiment 3								
Component B (004-001) 4 µg								
Day 9		*Day 11*		*Day 14*		*Day 16*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0.138	-84.0647	0.008	-99.0762	0	-100	0	-100	
0.264	-65.1255	0.135	-82.1664	0.042	-94.4518	0	-100	
0.173	-78.3479	0.081	-89.8623	0	-100	0	-100	
0.212	-73.8272	0.082	-89.8765	0	-100	0	-100	
Mean ± S.D.								
0.219	-71.989	0.093	-88.044	0.007	-99.079	0.000	-100.000	
0.053	7.837	0.049	6.662	0.014	1.817	0.000	0.000	
Day 18		*Day 21*		*Day 23*				
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*			
0	-100	0	-100	0	-100			
0	-100	0	-100	0	-100			
0	-100	0	-100	0	-100			
0	-100	0	-100	0	-100			
0	-100	0	-100	0	-100			
0	-100	0	-100	0	-100			
0	-100	0	-100	0	-100			
0	-100	0	-100	0	-100			
0	-100	0	-100	0	-100			
0	-100	0	-100	0	-100			
Mean ± S.D.								
0	100.000	0	-100	0	-100			

Table 3C: (continued)

Wound healing data - Experiment 3								
Component B (004-001) 4 µg								
Day 18		Day 21			Day 23			
area	% variat.	area	% variat.		area	% variat.		
0.000	0.000	0.000	0.000		0.000	0.000		

Table 3D:

Wound healing data - Experiment 3								
Component B (004-001) 2μg								
Day 0	*Day 1*		*Day 3*		*Day 5*		*Day 7*	
area	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.776	0.591	-23.8402	0.577	-25.6443	0.285	-63.6943	0.202	-74.2675
0.785	0.548	-30.1911	0.447	-43.0573	0.357	-53.9948	0.309	-60.1804
0.776	0.68	-12.3711	0.587	-24.3557	0.435	-44.0874	0.319	-58.9974
0.778	0.498	-35.990	0.194	-75.0643	0.179	-76.933	0.112	-85.567
0.776	0.428	-44.845	0.183	-76.4175	0.152	-81.071	0.092	-88.543
0.803	0.638	-20.548	0.597	-25.6538	0.427	-44.183	0.365	-52.2876
0.765	0.72	-5.882	0.657	-14.1176	0.496	-41.3018	0.357	-57.7515
0.845	0.591	-30.059	0.512	-39.4083	0.427	-47.284	0.337	-58.3951
0.81	0.669	-17.407	0.567	-30	0.518	-36.0494	0.355	-56.1728
0.834	0.631	-24.341	0.469	-43.765	0.316	-60.2416	0.233	-70.6844
Mean ± S.D.								
0.7948	0.599	-24.547	0.479	-39.748	0.359	-54.884	0.268	-66.285
0.027	0.089	11.398	0.165	21.0968	0.359	15.301	0.268	12.797

Day 9		*Day 11*		*Day 14*		*Day 16*	
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.173	-77.7062	0.063	-91.8814	0	-100	0	-100
0.229	-70.828	0.093	-88.1529	0	-100	0	-100
0.246	-68.299	0.056	-92.7835	0.007	-99.0979	0	-100
0.107	-86.2468	0	-100	0	-100	0	-100
0.008	-98.9691	0	-100	0	-100	0	-100
0.141	-82.4408	0.08	-90.0374	0	-100	0	-100

Table 3D: (continued)

Wound healing data - Experiment 3							
Component B (004-001) 2μg							
Day 9		*Day 11*		*Day 14*		*Day 16*	
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.316	-58.6928	0.181	-76.3399	0.114	-85.098	0	-100
0.196	-76.8047	0.086	-89.8225	0	-100	0	-100
0.28	-65.4321	0.188	-76.7901	0.106	-86.9136	0.053	-93.4568
0.153	-81.1111	0.008	-99.0408	0	-100	0	-100
Mean ± S.D.							
0.185	-76.653	0.076	-90.485	0.023	-97.111	0.005	-99.346
0.090	11.531	0.067	8.532	0.046	5.875	0.017	2.069

Day 18		*Day 21*		*Day 23*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
0	-100	0	-100	0	-100	
Mean ± S.D.						
0.000	-100.000	0.000	-100.000	0.000	-100.000	

Table 3D: (continued)

Wound healing data - Experiment 3						
Component B (004-001) 2µg						
Day 18		*Day 21*		*Day 23*		
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	
0.000	0.000	0.000	0.000	0.000	0.000	

Table 3E:

Wound healing data - Experiment 3								
Component B (004-001) 1mg/kg, i.v.								
Day 0	*Day 1*		*Day 3*		*Day 5*		*Day 7*	
area	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.702	0.532	-24.2165	0.233	-66.8091	0.159	-77.3504	0.18	-74.359
0.713	0.545	-23.5624	0.401	-43.7588	0.321	-54.979	0.311	-56.3815
0.854	0.731	-14.4028	0.608	-28.8056	0.447	-47.6581	0.43	-49.6487
0.698	0.597	-14.470	0.421	-39.6848	0.321	-54.0115	0.297	-57.4499
0.702	0.591	-15.812	0.459	-34.6154	0.329	-53.1339	0.301	-57.1225
0.791	0.529	-33.123	0.433	-45.2592	0.329	-58.4071	0.263	-66.7509
0.799	0.611	-23.529	0.387	-51.5645	0.231	-71.0889	0.113	-85.8573
0.842	0.791	-6.057	0.462	-45.1306	0.418	-50.3563	0.352	-58.1948
0.834	0.628	-24.700	0.481	-42.3261	0.393	-52.8777	0.311	-62.7098
0.886	0.818	-7.675	0.694	-21.6704	0.55	-37.9233	0.54	-39.0519
Mean ± S.D.								
0.7821	0.637	-18.755	0.458	-41.962	0.350	-55.779	0.310	-60.753
0.072	0.106	8.482	0.125	12.373	0.110	11.255	0.119	12.906

Day 9		*Day 11*		*Day 14*		*Day 16*	
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.106	-84.9003	0.012	-98.2906	0	-100	0	-100
0.229	-67.8822	0.088	-87.6578	0	-100	0	-100
0.324	-62.0609	0.127	-85.1288	0.007	-99.1803	0.008	-99.0632
0.204	-70.7736	0.027	-96.1318	0	-100	0	-100
0.137	-80.4843	0.043	-93.8746	0	-100	0	-100
0.137	-82.6802	0.008	-98.9886	0	-100	0	-100

Table 3E: (continued)

Wound healing data - Experiment 3							
Component B (004-001) 1mg/kg, i.v.							
Day 9		*Day 11*		*Day 14*		*Day 16*	
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.053	-93.3667	0	-100	0	-100	0	-100
0.307	-63.5392	0.138	-83.6105	0.011	-98.6936	0	-100
0.2	-76.0192	0.072	-91.3669	0	-100	0	-100
0.39	-55.9819	0.212	-76.0722	0.013	-98.5327	0	-100
Mean ± S.D.							
0.209	-73.769	0.073	-91.112	0.003	-99.641	0.001	-99.906
0.106	11.734	0.069	7.858	0.005	0.600	0.003	0.296
Day 18		*Day 21*		*Day 23*			
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*		
0	-100	0	-100	0	-100		
0	-100	0	-100	0	-100		
0	-100	0	-100	0	-100		
0	-100	0	-100	0	-100		
0	-100	0	-100	0	-100		
0	-100	0	-100	0	-100		
0	-100	0	-100	0	-100		
0	-100	0	-100	0	-100		
0	-100	0	-100	0	-100		
0	-100	0	-100	0	-100		
Mean ± S.D.							
0.000	-100.000	0.000	-100.000	0.000	-100.000		

Table 3E: (continued)

Wound healing data - Experiment 3									
Component B (004-001) 1mg/kg, i.v.									
Day 18		Day 21			Day 23				
area	% variat.	area	% variat.		area	% variat.			
0.000	0.000	0.000	0.000		0.000	0.000			

Table 4A:

Wound healing data - Experiment 4								
Phosphate buffer								
Day 0	*Day 1*		*Day 3*		*Day 5*		*Day 7*	
area	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.813	0.817	0.492005	0.785	-3.44403	0.393	-51.6605	0.297	-63.4686
0.813	0.809	-0.492	0.817	0.492005	0.462	-43.1734	0.541	-33.4563
0.954	0.981	2.830189	0.912	-4.40252	0.672	-29.5597	0.584	-38.7841
0.833	0.821	-1.441	0.716	-14.0456	0.48	-42.377	0.404	-51.5006
0.841	0.882	4.875	0.878	4.399524	0.758	-9.8692	0.694	-17.4792
0.813	0.805	-0.984	0.608	-25.2153	0.407	-49.9385	0.393	-51.6605
0.805	0.821	1.988	0.746	-7.32919	0.544	-32.4224	0.444	44.8447
0.769	0.825	7.282	0.762	-0.91027	0.69	-10.2731	0.657	-14.5644
0.845	0.874	3.432	0.845	0	0.639	-24.3787	0.636	-24.7337
0.817	0.829	1.469	0.789	-3.42717	0.496	-39.2901	0.387	-52.6316
Mean ± S.D.								
0.830	0.846	1.945	0.786	-5.388	0.554	-33.294	0.504	-39.312
0.8303	0.054	2.757	0.087	8.563	0.127	14.919	0.136	16.428

Day 9		*Day 11*		*Day 14*		*Day 16*	
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.269	-66.9127	0.173	-78.7208	0.125	-84.6248	0.091	-88.8069
0.3	-63.0996	0.19	-76.6298	0.182	-77.6138	0.062	-92.3739
0.481	-49.5807	0.407	-57.3375	0.365	-61.74	0.227	-76.2055
0.345	-58.5834	0.264	-68.3073	0.239	-71.3085	0.112	-86.5546
0.522	-37.931	0.271	-67.7765	0.173	-79.4293	0.137	-83.7099
0.283	-65.1907	0.289	-64.4526	0.168	-79.3358	0.124	-84.7478

Table 4A: (continued)

Wound healing data - Experiment 4							
Phosphate buffer							
Day 9		*Day 11*		*Day 14*		*Day 16*	
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.361	-55.1553	0.285	-64.5963	0.214	-73.4161	0.074	-90.8075
0.472	-38.6216	0.311	-59.5579	0.271	-64.7594	0.155	-79.844
0.374	-55.7396	0.352	-58.3432	0.264	-68.7574	0.148	-82.4852
0.246	-69 8898	0.261	-68.0539	0.19	-76 7442	0.112	-86.2913
Mean ± S.D.							
0.365	-56.070	0.280	-66.378	0.219	-73.773	0.124	-85.183
0.097	11.175	0.069	7.193	0.069	7.162	0.047	4.925
Day 18		*Day 21*		*Day 23*			
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*		
0.071	-91.2669	0.009	-98.893	0	-100		
0.044	-94.5879	0	-100	0	-100		
0.099	-89.6226	0.27	-71.6981	0	-100		
0.072	-91.3565	0	-100	0	-100		
0.092	-89.0606	0.031	-96.3139	0	-100		
0.069	-91.5129	0	-100	0	-100		
0.043	-94.6584	0	-100	0	-100		
0.031	-95.9688	0.28	-63.5891	0	-100		
0.047	-94.4379	0	-100	0	-100		
0.066	-91.9217	0.008	-99.0208	0	-100		
Mean ± S.D.							
0.063	-92.439	0.060	-92.951	0.000	-100.000		

Table 4A: (continued)

Wound healing data - Experiment 4								
Phosphate buffer								
Day 18		*Day 21*		*Day 23*				
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*			
0.022	2.334	0.114	13.522	0.000	0.000			

Table 4B:

Wound healing data - Experiment 4								
Bovine Serum Albumin								
Day 0	*Day 1*		*Day 3*		*Day 5*		*Day 7*	
area	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.785	0.821	4.585987	0.805	2.547771	0.765	-2.54777	0.622	-20.7643
0.857	0.858	0.116686	0.786	-8.28471	0.65	-24.154	0.625	-27.0712
0.837	0.874	4.42055	0.825	-1.43369	0.746	-10.8722	0.544	-35.006
0.781	0.817	4.609475	0.794	1.664533	0.708	-9.34699	0.611	-21.767
0.853	0.924	8.323564	0.882	3.399766	0.735	-13.8335	0.668	-21.6882
0.845	0.895	5.91716	0.785	-7.10059	0.727	-13.9645	0.618	-26.8639
0.833	0.893	7.202881	0.878	5.402161	0.675	-18.9676	0.453	-45.6182
0.854	0.916	7.259953	0.899	5.269321	0.712	-16.6276	0.48	-43.7939
Mean ± S.D.								
0.831	0.875	5.305	0.832	0.183	0.715	-13.789	0.578	-30.322
0.031	0.040	2.553	0.047	5.327	0.038	6.513	0.077	9.993

Day 9		*Day 11*		*Day 14*		*Day 16*	
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.538	-31.465	0.344	-56.1783	0.244	-68.9172	0.169	-78.4713
0.557	-35.0058	0.368	-57.0595	0.329	-61.6103	0.162	-81.0968
0.413	-50.6571	0.287	-65.7109	0.226	-72.9988	0.101	-87.9331
0.554	-29.0653	0.329	-57.8745	0.259	-66.8374	0.138	-82.3303
0.448	-47.4795	0.352	-58.7339	0.239	-71.9812	0.173	-79.7186
0.561	-33.6095	0.299	-64.6154	0.255	-69.8225	0.21	-75.1479
0.314	-62.3049	0.255	-69.3878	0.22	-73.5894	0.166	-80.072
0.404	-52.6932	0.266	-68.8525	0.239	-72.0141	0.166	-80.5621

Table 4B: (continued)

Wound healing data - Experiment 4							
Bovine Serum Albumin							
Day 9		*Day 11*		*Day 14*		*Day 16*	
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
Mean ± S.D.							
0.474	-42.785	0.313	-62.302	0.251	-69.721	0.161	-80.667
0.092	12.097	0.042	5.443	0.034	3.979	0.031	3.631
Day 18		*Day 21*		*Day 23*		*Day 25*	
area	*% variat.*	*area*	*% variat.*	*area*	*% variat.*	*area*	*% variat.*
0.062	-92.1019	0.007	-99.1083	0	-100	0	-100
0.039	-95.4492	0.021	-97.5496	0	-100	0	-100
0	-100	0.000	-100	0	-100	0	-100
0.081	-89.6287	0.031	-96.0307	0	-100	0	-100
0.094	-88.9801	0.055	-93.5522	0.018	-97.8898	0	-100
0.145	-82.8402	0	-100	0	-100	0	-100
0.083	-90.036	0.008	-99.0396	0	-100	0	-100
0.107	-87.4707	0	-100	0	-100	0	-100
Mean ± S.D.							
0.076	-90.813	0.015	-98.160	0.002	-99.736	0.000	-100.000
0.044	5.178	0.020	2.329	0.006	0.746	0.000	0.000

Claims

1. Use of Component B for the manufacture of a medicament useful as cicatrizant.

2. Use of component B for the manufacture of a medicament for use in the treatment of wounds, ulcers and traumatic lesions to tissues of the body.

3. The use according to Claims 1 or 2 wherein the medicament is to be used in the treatment of surgical wounds.

Patentansprüche

1. Verwendung von Komponente B zur Herstellung eines Arzneimittels, das als Wundheilungsmittel verwendbar ist.

2. Verwendung von Komponente B zur Herstellung eines Arzneimittels zur Verwendung bei der Behandlung von Wunden, Geschwüren und traumatischen Läsionen bei Körpergeweben.

3. Verwendung nach Ansprüchen 1 oder 2, wobei das Arzneimittel bei der Behandlung von Operationswunden anzuwenden ist.

Revendications

1. Utilisation du Composant B pour la fabrication d'un médicament utile comme cicatrisant.

2. Utilisation du Composant B pour la fabrication d'un médicament destiné à être utilisé dans le traitement des blessures, des ulcères et des lésions traumatiques des tissus du corps.

3. Utilisation selon la revendication 1 ou 2, dans laquelle le médicament est destiné à être utilisé dans le traitement de blessures chirurgicales.

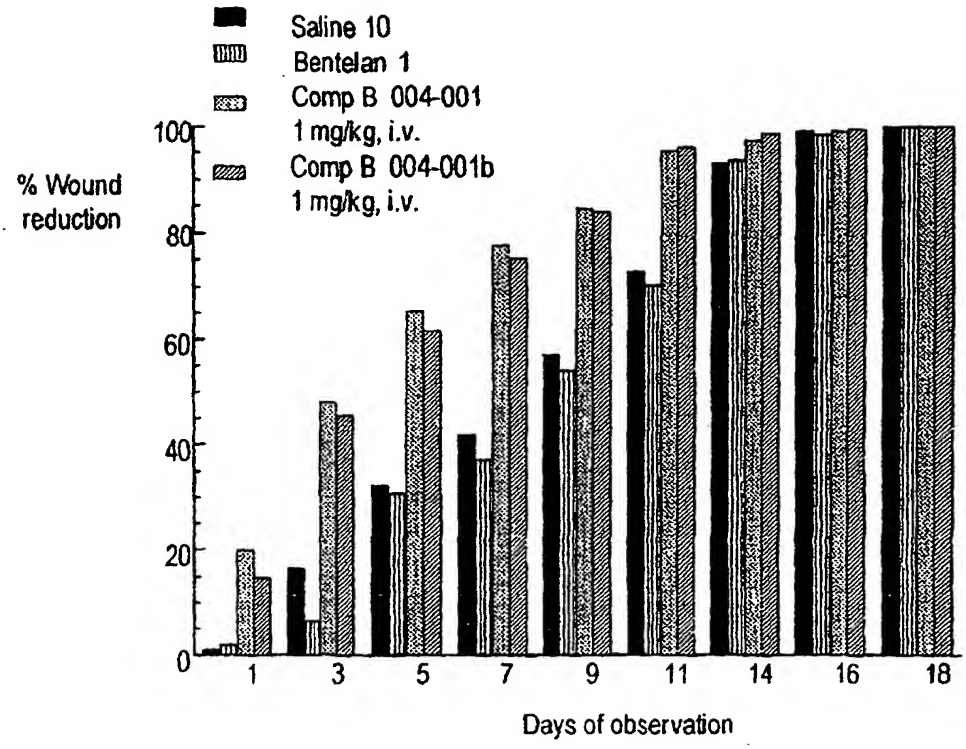
Saline 10
Bentelan 1
Comp B 004-001
1 mg/kg, i.v.
Comp B 004-001b
1 mg/kg, i.v.
% Wound reduction
100
80
60
40
20
0
1
3
5
7
9
11
14
16
18
Days of observation

Figure 1

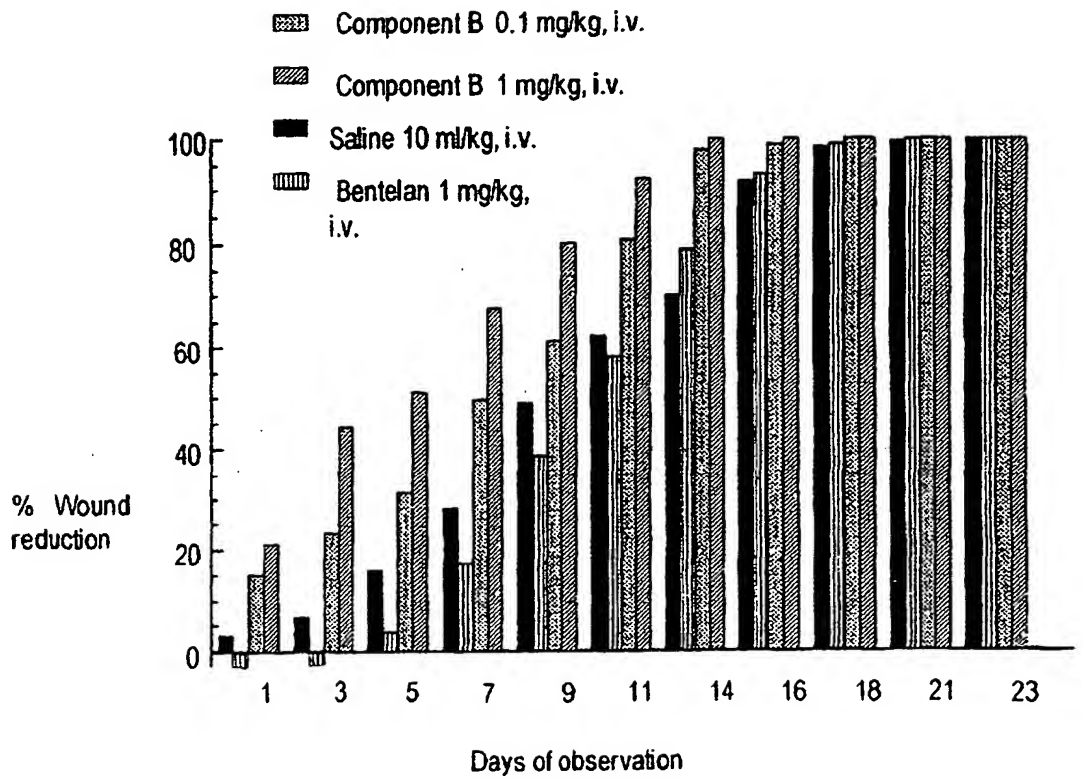
Component B 0.1 mg/kg, i.v.
Component B 1 mg/kg, i.v.
Saline 10 ml/kg, i.v.
Bentelan 1 mg/kg, i.v.
% Wound reduction
100
80
60
40
20
0
1
3
5
7
9
11
14
16
18
21
23
Days of observation

Figure 2

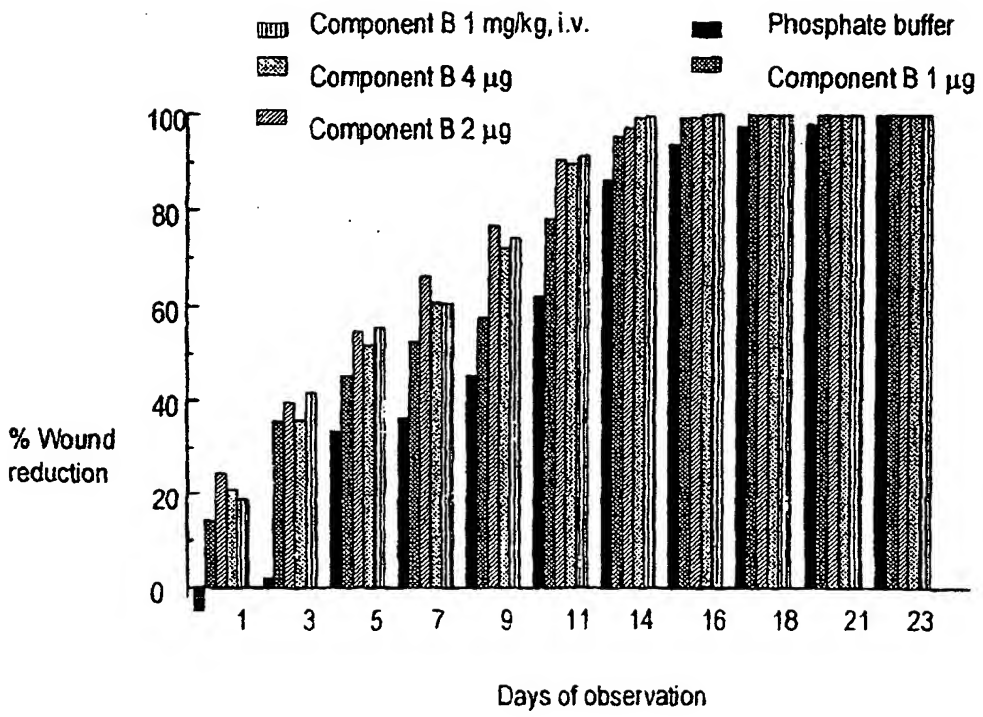
Component B 1 mg/kg, i.v.
Component B 4 µg
Component B 2 µg
Phosphate buffer
Component B 1 µg
% Wound reduction
100
80
60
40
20
0
1
3
5
7
9
11
14
16
18
21
23
Days of observation

Figure 3

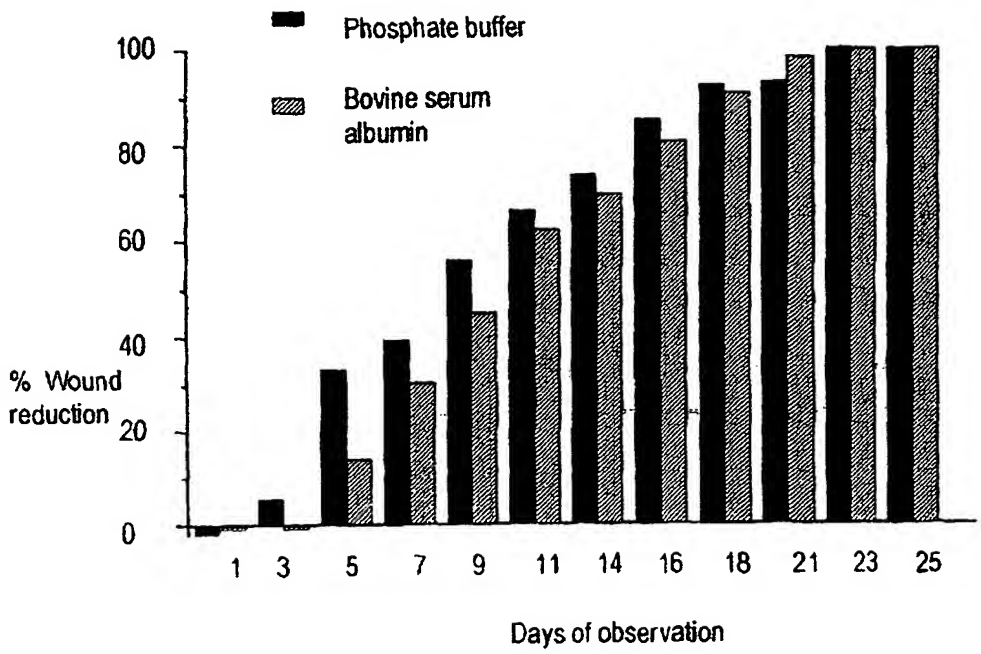
Phosphate buffer
Bovine serum albumin
100
80
60
40
20
0
% Wound reduction
1
3
5
7
9
11
14
16
18
21
23
25
Days of observation

Figure 4

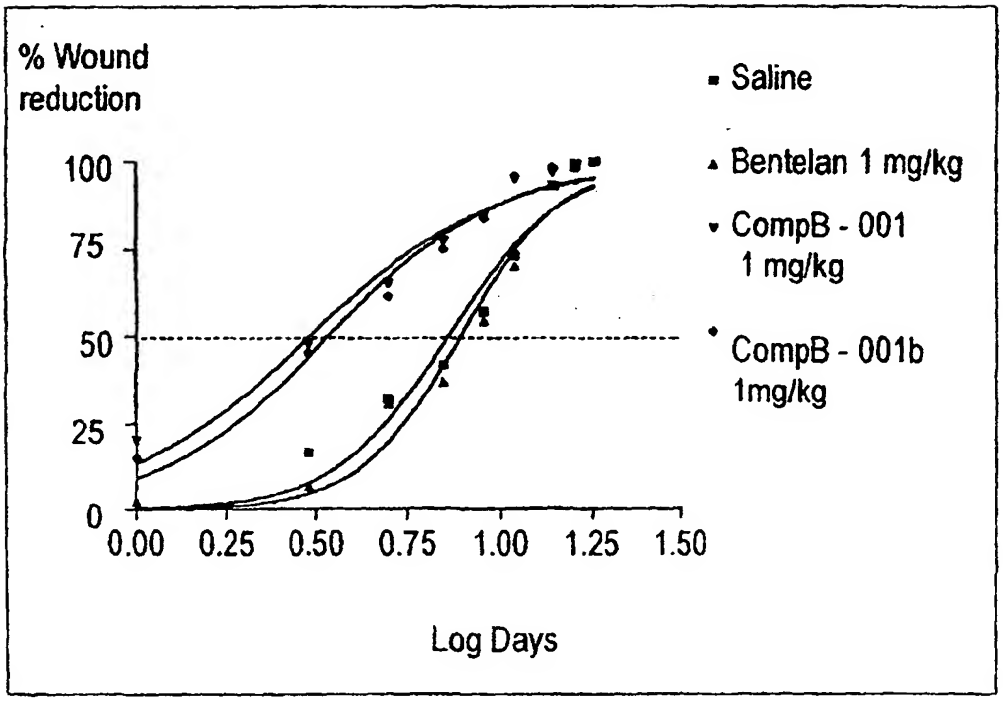
% Wound reduction
100
75
50
25
0
0.00
0.25
0.50
0.75
1.00
1.25
1.50
Log Days
Saline
Bentelan 1 mg/kg
CompB - 001 1 mg/kg
CompB - 001b 1mg/kg

Figure 5

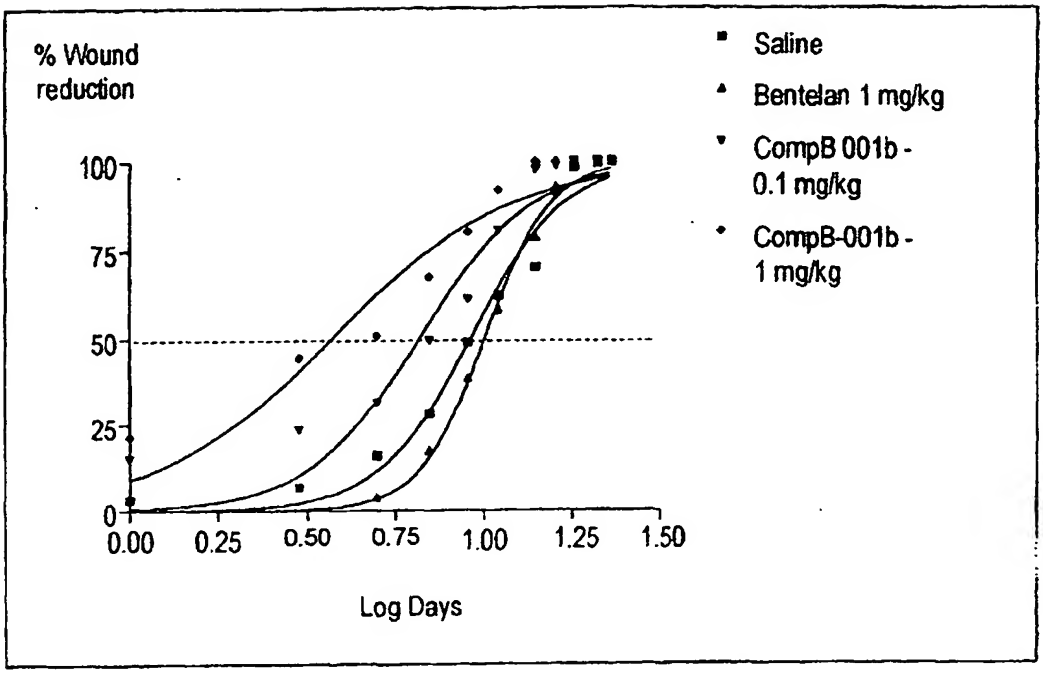
% Wound reduction
100
75
50
25
0
0.00
0.25
0.50
0.75
1.00
1.25
1.50
Log Days
Saline
Bentelan 1 mg/kg
CompB 001b - 0.1 mg/kg
CompB-001b - 1 mg/kg

Figure 6

Wound area

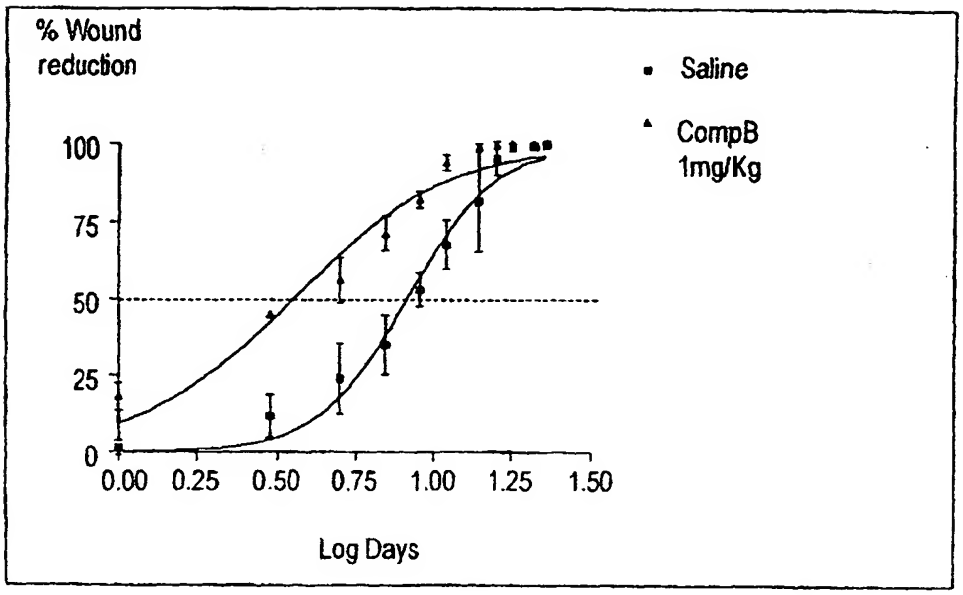

Figure 7

Cumulative Frequency

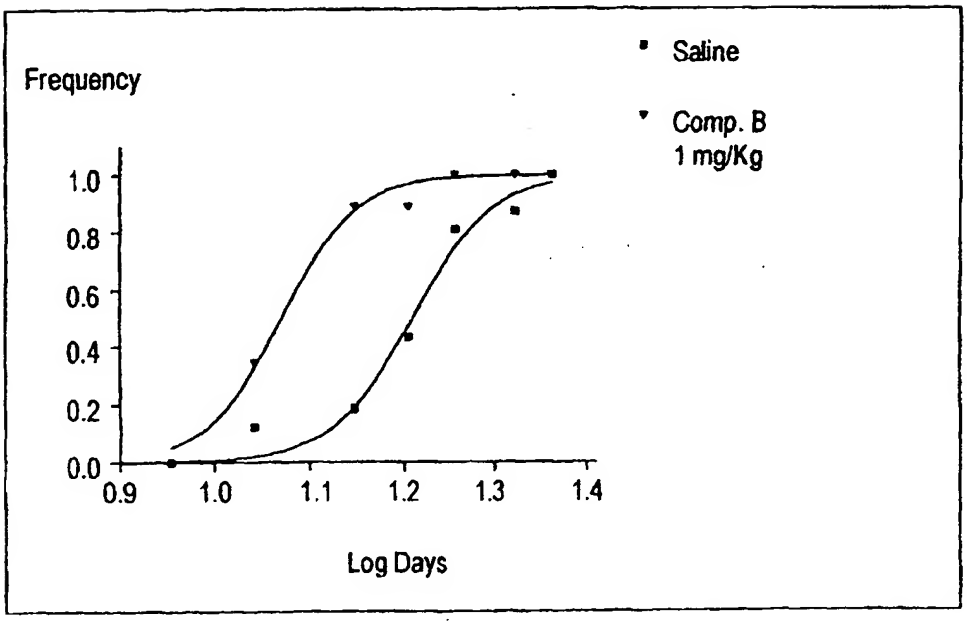

Figure 8

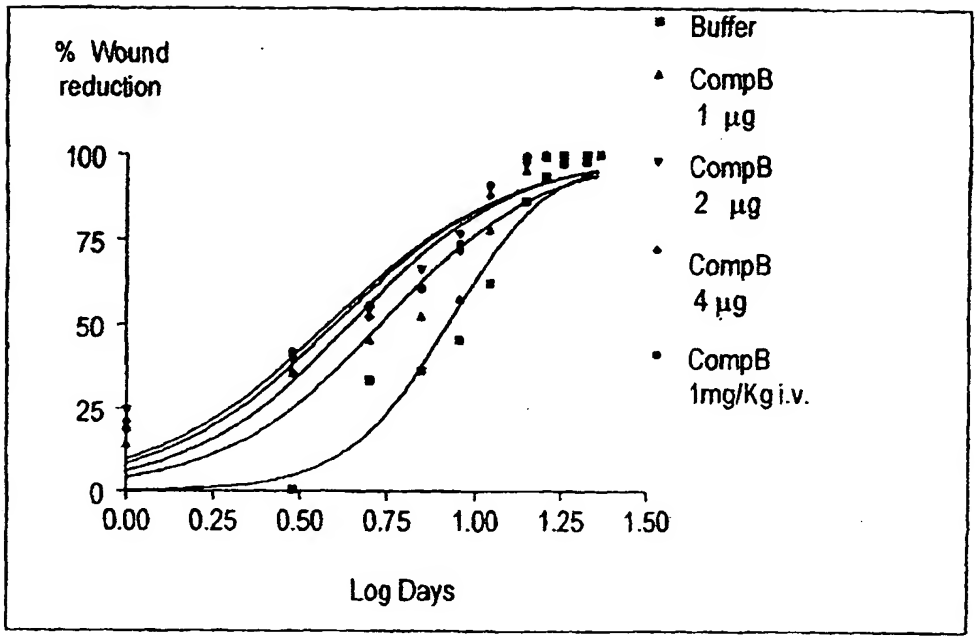
% Wound reduction
100
75
50
25
0
0.00
0.25
0.50
0.75
1.00
1.25
1.50
Log Days
Buffer
CompB 1 µg
CompB 2 µg
CompB 4 µg
CompB 1mg/Kg i.v.

Figure 9

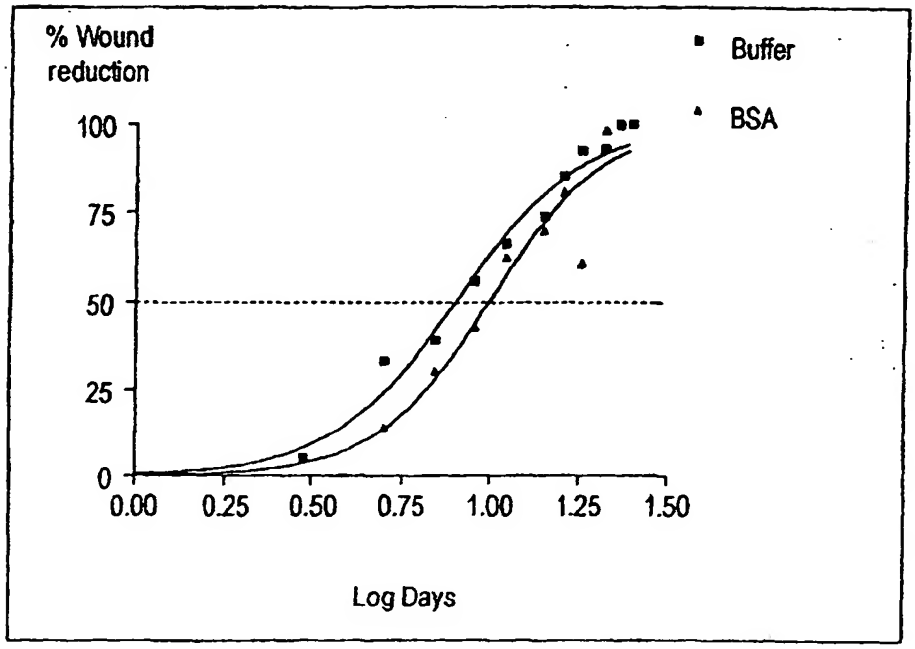
% Wound reduction
Buffer
BSA
100
75
50
25
0
0.00
0.25
0.50
0.75
1.00
1.25
1.50
Log Days

Figure 10